REMARKS/ARGUMENTS

Claims 17-23 and 30-44 are pending. No amendments are being made. All claims were examined and rejected over newly cited application 2003/0120297 to Beyerlein optionally in combination with newly cited publication 2005/0090714 to Greff. Such rejections are respectfully traversed for the reasons discussed below.

Claim 17, the only pending independent claim, reads as follows:

> 17. An improved method for injecting a pharmaceutical agent into the tissue of a living host using a needle positioned from a lumen of a blood vessel, wherein the improvement comprises:
>
> positioning the needle outwardly from the blood vessel lumen through the blood vessel wall and past an external elastic lamina (EEL);
>
> **confirming that a delivery aperture of the needle has penetrated into tissue beyond the external elastic lamina (EEL) of the blood vessel;** and
>
> injecting the pharmaceutical agent through the needle into the tissue after it has been confirmed that the aperture of the needle is positioned beyond the external elastic lamina (EEL).

As described in the present application, in previous responses, and in a prior in-person interview with the Examiner, the essence of the present invention is that the location of the needle aperture is confirmed prior to injecting a pharmaceutical agent into the tissue beyond the external elastic lamina.

The Examiner relies on the teachings of Beyerlein '297 in Fig. 2 as disclosing "a method for injecting a pharmaceutical agent beyond the EEL of a coronary blood vessel by 5 mm or less **and confirming the position of the needle.**" Applicants respectfully disagree with this characterization.

While Beyerlein does recognize the desirability of injection beyond the EEL, the Beyerlein device and method confirm only that an injection needle has been fully extended to a a predetermined needle length, not that the needle has in fact reached tissue beyond the EEL. As

described in Beyerlein, the needle deployment assembly comprises sensors which can detect when the needle has been fully extended to a desired depth, anywhere from 0.25 mm to 4 cm. See Paragraph 44. The needle mechanism includes a sensor for assuring that the needle has been extended to its full length (see Paragraph 56), but nowhere does Beyerlein teach confirmation that the needle has reached the tissue beyond the EEL.

While Applicants recognize that it might be possible to choose a depth, e.g. 4 cm, which would always achieve penetration beyond the EEL, the use of an excessively long fixed length has many disadvantages. Not only is it difficult to introduce and deploy such a long needle, the needle may extend into regions where it is not intended to be placed. For example, if the desired intent is to treat a coronary artery by delivering drug into the adventitia and thin layer of connective tissue outside the EEL, a needle that is so long as to penetrate through the EEL in every vessel would very likely penetrate through the adventitia and connective tissue as well, and into the myocardium or pericardial fluid. Such a delivery would, at least, be ineffective for treatment of the coronary artery and could be dangerous if the drug is delivered into tissue for which it is not indicated. Similarly, if the intent is to treat a peripheral artery in the leg by infusing drug into the adventitia and connective tissue, a fixed-length needle that would penetrate beyond the EEL of every artery would likely deposit the drug into the leg muscle most of the time, rather than the target connective tissue.

The Examiner should appreciate that the distance between the luminal wall and the external elastic lamina (EEL) may vary considerably, typically from 0.4 mm to 1.0 mm, for example, in coronary/carotid arteries[de Groot E, Hoving GK, Wiegman A, Duriez P, Smit AJ, Fruchart JC, Kastelein JJP, *Measurement of Arterial Wall Thickness as a Surrogate Marker for Atherosclerosis*, Circulation 2004;109:33-38.], and up to 3 mm or more when heavy plaque burden is present in the vessel. Under such circumstances, according to the present invention, a needle having a fixed (but not excessive) length which is likely to penetrate past the EEL may be used. Should the needle be initially located at a point where the distance to the EEL exceeds the needle length, such failure will be revealed in the confirming step of the present invention, and the needle can then be repositioned to a region having a different distance to the EEL and deployed. By confirming that the needle aperture has in fact passed the EEL, delivery of the

drug to the desired tissue can always be assured without the need to employ an excessively long needle which would be the case with the devices and systems of Beyerlein.

For these reasons, Applicants submit that Beyerlein does not anticipate the limitations of claim 17. In particular, Beyerlein neither teaches nor suggests that the position of the needle aperture be confirmed before injecting the pharmaceutical agent. Indeed, such a step is contraindicated since Beyerlein teaches that it is sufficient to use a long needle and confirm only that the needle is fully deployed prior to delivering the pharmaceutical agent.

Claim 18 was rejected over the combination of Beyerlein as modified by Greff. The Examiner concedes that Beyerlein does not teach the step of injecting contrast media through a needle aperture and observing the distribution of media to confirm needle position, relying on Greff for that teaching.

Applicants respectfully traverse this combination. First, Beyerlein never teaches that the position of the needle aperture beyond the EEL be confirmed, only that the full deployment of the needle be confirmed. The use of contrast media as taught by Greff would not meet the requirements of Beyerlein where a mechanical and/or electrical confirmation of needle deployment is taught. Moreover, Greff cannot be relied on to suggest confirming the needle position in Beyerlein since Beyerlein teaches that only needle deployment need be confirmed, not needle position as claimed herein. Indeed, it is difficult to envision how contrast media could be used to confirm full needle deployment, which is the purpose of Beyerlein.

For these reasons, Applicants believe that independent claim 17 as well as all claims dependent thereon distinguish over the teachings of Beyerlein even when combined with those of Greff.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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